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DIAZOMETHANE FROM THE REACTION OF HYDRAZINE WITH DICHLOROCARBENE - CROWN ETHER PTC CATALYSIS

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Over sixty years ago Staudinger and Küpfer reported that diazomethane could be prepared in 25% yield by the reaction of hydrazine with chloroform and base in ethanol solvent.[1] However, despite the fact that hydrazine is quite inexpensive, this procedure is seldom used. Diazomethane is generally prepared in about 75% yield by treatment of one of the following N-methyl-N-nitrosamides with base: bis-(N-methyl-N-nitroso)terephthalamide,[2] p-toluenesulfonylmethylnitrosamide,[3] N-methyl N'-nitro-N-nitrosoguanidine,[4] N-nitrosomethylurea,[5] or N,N'-dinitroso-N,N'-dimethyloxamide.[6] In addition to cost, certain of these precursors have the added disadvantage that they must be stored at low temperature and that they are carcinogenic.

We should like to report that diazomethane can routinely be generated in 48% yield by the reaction of hydrazine hydrate with chloroform and potassium hydroxide in ether solvent by addition of catalytic amounts of 18-crown-6 ether [7-9] as a phase transfer catalyst (PTC). A lower yield (35%) was obtained using sodium hydroxide as base. Quarternary ammonium salt PTC catalysts such as tetrabutylammonium bromide also yield diazomethane in approximately 35% yield using either sodium or potassium hydroxide as base.

Experimental: All the usual precautions for working with diazomethane were observed,[2] including the use of an efficient hood. The reaction was conducted in a 500 ml round bottom two neck flask. To the vertical neck was sealed a 3 x 28 cm column, the lower 18 cm of which was Vigreuxed. A side arm was connected at the top of the Vigreuxed region. The second, short neck was used to add reagents and a stirring bar. The side arm was connected to a West condenser to which was attached a bent adapter reaching almost to the bottom of a 500 ml ice-cooled Erlenmeyer receiver flask, charged initially with 50 ml of ether. A 250 ml addition funnel was connected to the top of the column. The reaction flask was charged with 80 g (1.4 mol) of potassium hydroxide pellets, 20 ml of water, 48 g (0.4 mol) of chloroform, 200 ml of ether, 0.2 g (0.8 mmol) of 18-crown-6 ether, and finally 11.76 g (0.2 mol) of 85% hydrazine hydrate. The second neck was stoppered with a rubber stopper. The reaction mixture was heated and vigorously stirred. The reaction mixture slowly (approximately 15 minutes) becomes yellow. As the reaction proceeds it foams and the distillate becomes distinctly yellow colored. When 100 ml of distillate has been collected fresh ether is added to the reaction flask from the addition funnel at a rate equal to the rate of the distillation. In this manner, the volume of ether in the reaction flask is maintained at approximately 100 ml throughout the course of the reaction. The reaction is continued until no further color is observed in the distillate (400-600 ml). The quantity of diazomethane was determined by reaction with benzoic acid to yield methyl benzoate. A 48% ± 4 (16 runs) yield based on hydrazine added was obtained. Addition of extra 18-crown-6 ether had no effect on the yield but did markedly increase the rate and the exothermicity of the reaction. In addition 3.0-4.0 g of hydrazinium benzoate was obtained. This is probably due to azeotropic distillation of hydrazine since use of a longer Vigreuxed neck (45 cm) made little difference. Clearly this will limit use of this procedure to those who can tolerate a small amount of hydrazine in their ethereal diazomethane solutions. Alternatively, methylene chloride can be substituted for ether. The hydrazine impurity (less than half the amount obtained with ether) can be removed by extraction of the diazomethane methylene chloride solution (250 ml) with water (25 ml). A 38% yield of diazomethane free of hydrazine was obtained in this way.

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